The Intercontinental Journal of Emergency Medicine

Original Article

DOI: 10.51271/ICJEM-0018

The effect of neutrophil lymphocyte ratio and other biochemical parameters on mortality in cancer patients admitted to the emergency department

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Cite this article: Okay NG, Kibici Ö, Erdoğan MÖ. The effect of neutrophil lymphocyte ratio and other biochemical parameters on mortality in cancer patients admitted to the emergency department. *Intercont J Emerg Med*. 2023;1(4):67-70.

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Received: 24/11/2023 ◆ **Accepted**: 18/12/2023 ◆ **Published**: 30/12/2023

ABSTRACT

Aims: To investigate the effectiveness of the neutrophil/lymphocyte ratio and other biochemical parameters in predicting mortality in oncology patients with cancer admitted to the emergency department.

Methods: This was a retrospective, observational, single-center study. The study period included a two-year period from January 2014 to December 2015. Demographic data, cancer history and blood tests, emergency department diagnoses, blood parameters evaluated in the emergency department, discharge, and mortality status of the patients were recorded in the data form. The APACHE 2 and SOFA scores of all patients were also calculated. Patients whose data could not be reached were excluded from the study. p<0.05 was considered statistically significant.

Results: A total of 180 patients were included in the study. The mean age of the survivor group was 66.4±10.752 years, while the mean age of the non-survivor group was 65.18±13 years. The mean neutrophil/lymphocyte (NLR) ratio of the non-survivor group was 1.0288±11.3, while the NLR of the survivor group was 4.400±3.563. (p<0.05) The mean lactate ratio of the non-survivor group was 2.60±3.384, while the mean lactate ratio of the survivor group was 1.36±1. 090. (p<0.05) When survivor and non-survivor patient groups were compared, a statistically significant difference was observed in mean white blood cell count, neutrophil count, hemoglobin, hematocrit, and blood urea nitrogen (BUN) values. (p<0.05)

Conclusion: According to the results of this study, NLR, elevated white blood cell and neutrophil values, decreased hemoglobin and hematocrit, and elevated BUN and lactate levels seem to be predictors of mortality during emergency admissions in cancer patients.

Keywords: Mortality, oncology, emergency department, blood tests

INTRODUCTION

Cancer is the non-survival or abnormal growth and proliferation of cells as a result of DNA damage. Cancer is an umbrella term of disorders characterized by the loss of typical tissue features, uncontrolled cell growth, and the ability to invade nearby tissues and distant organs.[1] There are over 200 diseases in this group histopathologically. Cancer patients may succumb to secondary complications that might be fatal, in addition to their initial ailment. The aforementioned conditions include infection, sepsis, hemorrhages, thromboembolic events, as well as single and multiple organ failure.[2] At the same time, neutropenic fever and sepsis are important problems in cancer patients, and their mortality rates are as high as 40-70% if they are not treated appropriately without losing time.[3]

An increased neutrophil-to-lymphocyte ratio (NLR) has also been found to be an indicator of poor prognosis in patients undergoing cardiovascular intervention. Recent studies have shown a correlation between elevated NLR (neutrophil-to-lymphocyte ratio) and higher fatality rates in cases of acute coronary syndromes.[4,5] Studies have shown that NLR is a predictive indicator for survival in patients with colorectal and ovarian cancer.[6,7] It has been suggested that preoperative NLR may be a simple method to identify patients with poor prognosis in colorectal cancer.[8] NLR in peripheral blood is used as a parameter that provides information about the relationship between the inflammatory environment and physiological stress.

APACHE II, which is a combination of the total acute physiology score, age, and chronic health status scores, is assessed in the first 24 hours of ICU admission, with a maximum score of 71. When the total score is 25, the estimated mortality is 25%, whereas this increases to over 80% when the score is above 35.

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Emergency departments are the most frequent destination for oncology patients. With their twenty-four-hour accessibility, emergency departments are the first place these patients go in case of complications secondary to any kind of treatment. Evaluating the mortality expectancy of patients with simple examinations taken at emergency department visits can be used in clinical practice as a simple, fast, and inexpensive method. In this way, physicians can use more aggressive or alternative treatment modalities in complication management.

METHODS

This study is a retrospective, observational cohort study. The study period covers a two-year period between January 2014 and December 2015. Patients diagnosed with cancer and admitted to the emergency department of a tertiary care hospital were included in the study. This study is a specialty thesis in the field of emergency medicine. Before 2020, institutional approval was obtained, and ethics committee decisions were not taken for that period. The data on the patients was accessed from the hospital database. Patients whose data could not be accessed, who had incomplete information in their files, and who could not be examined in the emergency department were excluded from the study. The parameters analyzed from the records were age, gender, date of admission, type of cancer, metastases, treatment for cancer, reasons for admission to the emergency department, laboratory findings in the emergency department (white blood cells, neutrophils, lymphocytes, hemoglobin, hematocrit, blood urea nitrogen, creatine, sodium, potassium, ALT, AST, pH, bicarbonate, lactate), diagnosis in the emergency department, where they were transferred or discharged from the emergency department, and mortality. APACHE 2 and SOFA scores were also calculated for all patients. Patients were divided into two groups: survivors and non-survivors. The variables used in the study were statistically compared between these two groups.

Statistical Analysis

The data we obtained were analyzed with the Statistical Package for Social Sciences (SPSS) version 17.0 data analysis program. Student t tests for parametric data and chi-square tests for nonparametric data were used for data analysis. P<0.05 was considered statistically significant.

RESULTS

The study was completed with a total of 180 patients. While 107 patients had a history of surgical intervention, 73 patients had no history of surgical intervention. Patients presented to the emergency department with the most common complaint of shortness of breath (n=32), followed by pain (n=22), nausea, and vomiting (n=20). When the treatments received by the patients were examined, symptomatic treatment was the most common treatment in the emergency department, followed by pneumonia and anemia. While 86 of the patients were discharged from the emergency department, 41 were transferred to the internal medicine service, and 21 were transferred to the intensive care unit. Patients were analyzed as survivors and non-survivors according to their mortality status. The mean age of the survivor group was 66.4±10.752, and the mean age of the non-survivor group was 65.18±13. There was no statistically significant relationship between the two groups in terms of age (p=0.533). (**Table 1**) The mean WBC of the survivor group was 8.18±3.576, and the mean WBC of the non-survivor group was 12.9±8.233. There was a statistically significant relationship between the two groups in terms of WBC (p<0.05). The mean neutrophil count of the survivor group was 5.89±3.242, and the mean neutrophil count of the non-survivor group was 10.27±7.418. There was a statistically significant relationship between the two groups in terms of neutrophils (p<0.05). The mean lymphocyte count of the survivor group was 1.11±0.982, and the mean lymphocyte count of the non-survivor group was 1.10±1.522. There was no statistically significant relationship between the two groups in terms of lymphocytes (p=0.970). The mean NLR of the survivor group was 4.400±3.563, and the mean NLR of the non-survivor group was 1.0288±11.3. There was a statistically significant relationship between the two groups in terms of NLR (p<0.05).

Patients were also compared according to hemoglobin (HGB) and hematocrit (HTC) values. The mean HGB of the survivor group was 11.42±2.105, and the mean HGB of the non-survivor group was 9.85±2.254. There was a statistically significant relationship between the two groups in terms of HGB (p<0.05). The mean HTC of the survivor group was 35.62±5.859, and the mean HTC of the non-survivor group was 30.78±6.866. There was a statistically significant relationship between the two groups in terms of HTC (p<0.05).

Table 1. Descriptive characteristic of study participants

	Mortality	Mean	Standard Deviation	Standard Error Mean
Age	0	66.40	10.752	1.603
	1	65.18	13.000	1.119
White blood cell count 103/uL	0	8.18	3.576	0.533
	1	12.90	8.233	0.709
Neutrophil count 103/uL	0	5.89	3.242	0.483
	1	10.27	7.418	0.638
Lymphocyte count 103/uL	0	1.11	0.982	0.146
	1	1.10	1.522	0.131
NLR	0	4.400	3.563	0.531
	1	1.028	11.131	0.958
Hemoglobin g/dl	0	11.42	2.105	0.314
	1	9.85	2.254	0.194
Hematocrit %	0	35.62	5.859	0.873
	1	30.78	6.866	0.591
BUN mg/dl	0	21.93	11.963	1.783
	1	35.68	21.682	1.866
Creatinine mg/dl	0	0.71	1.854	0.276
	1	0.90	1.309	0.113
Alanine aminotranseraz U/L	0	33.40	55.794	8.317
	1	41.87	67.000	5.766
Aspartate aminotransferaz U/L	0	42.11	114.917	17.131
	1	71.31	148.811	12.808
Sodium mmol/L	0	137.00	4.447	0.663
	1	135.334	10.657	0.917
Potassium mmol/L	0	3.96	0.903	0.135
	1	4.01	0.846	0.073
pH	0	7.36	0.17	**0.000**
	1	7.32	0.54	**0.010**
Bicarbonate mmol/L	0	23.87	4.187	0.624
	1	22.31	5.963	0.513
Lactate mmol/L	0	1.36	1.090	0.163
	1	2.60	3.384	0.291

BUN: Blood urea nitrogen; NLR: Neutrophil lymphocyte rate

The mean BUN of the survivor group was 21.93±11.963, and the mean BUN of the non-survivor group was 35.68±21.682. In this comparison, a statistically significant relationship was found between the groups in terms of BUN ($p<0.05$). On the other hand, patients were also compared in terms of creatinine values. The mean creatinine of the survivor group was 0.71±1.854, and the mean creatinine of the non-survivor group was 0.90±1.309. There was no statistically significant relationship between the groups in terms of creatinine ($p>0.05$). The mean lactate of the survivor group was 1.36±1.090, and the mean lactate of the non-survivor group was 2.60±3.384. There was a statistically significant relationship between the two groups in terms of lactate ($p<0.05$).

DISCUSSION

In our study, we aimed to evaluate the efficacy of the sub-findings in the APACHE 2 scoring system and neutrophil lymphocyte ratio in predicting mortality in oncology patients. No difference was observed between the mortal and non-mortal groups in terms of findings such as age and gender. No difference was observed in terms of fever, mean arterial pressure, heart rate, respiratory rate, alveolar arterial oxygen gradients, pH, serum sodium, serum potassium, serum creatinine, and Glasgow coma scores.

Elevated white blood cell values, neutrophil counts, hematocrit values, BUN values, lactate values, and neutrophil-to-lymphocyte ratios were statistically significant. In addition, the patient's emergency admission secondary to colon cancer and hospitalization in the intensive care unit were also observed as predictors of mortality. At the same time, surgical operations for cancer were also observed as a predictor of mortality in our study.

White blood cell elevation is a parameter that is also present in APACHE 2 scoring and was found to be a predictor of mortality as an independent variable in our study group. White blood cell elevation is also present as a parameter in APACHE 2, which Knaus et al.[9] used in the APACHE 2 classification and is in routine use as a disease severity classification system. Our study is also compatible with this.

An elevated neutrophil count was found to be a predictor of mortality in our study and is usually associated with infections. It is also included in the total white blood cell count. Therefore, it may be considered secondary in the APACHE 2 scoring system. Therefore, as in this classification system indicating disease severity, neutrophil count was found to be a predictor of mortality in cancer patients in our study.

Low hemoglobin and hematocrit values were included in the APACHE 2 scoring system by Knaus et al.[9] In our study, low hemoglobin and hematocrit values were observed as predictors of mortality in cancer patients.

In our study, a high BUN value at the time of arrival to the emergency department was also observed as a predictor of mortality in cancer patients. The APACHE 2 scoring system includes creatinine elevation. However, APACHE 2 is a disease severity classification system. Our study, on the other hand, aimed to observe the mortality predictors of oncologic patients, which is a single disease group. Some differences between the two studies can be expected. Although the serum creatinine value was not significant in our study, it is part of the APACHE 2 scoring system. The elevated BUN value was significant in our study. Unfortunately, the fact that our study group was limited to 145 patients, i.e., a small niche-specific study group, does not allow us to determine every parameter that may be significant. The development of acute renal failure is a factor that increases mortality. It is plausible that increased BUN and creatinine, which are parameters of this picture, are predictors of mortality.

Lactate is used as a predictor of mortality through lactate clearance, especially in sepsis patients. It is even used to evaluate the effectiveness of early goal-directed therapy in sepsis patients. In our study, lactate was observed as a predictor of mortality in oncology patients. Husain et al.[10] examined lactate levels at baseline and 24 hours in their study of surgical intensive care unit patients and found a significant relationship between high serum lactate levels and mortality. Holtfreter et al.[11] found a statistically significant high lactate level in patients with exitus in their study conducted in an intensive care unit. Brain et al.[12] found that a high lactate level was associated with mortality in patients with infection. In our study, a statistically significant relationship was found between high serum lactate levels and mortality in cancer patients admitted to the emergency department, and a high serum lactate level was observed as a predictor of mortality.

The neutrophil-lymphocyte ratio, which is another significant finding, has been investigated in many studies in terms of the evaluation of disease severity. The physiologic response of circulating leukocytes to stress is an increase in neutrophils and a decrease in lymphocytes, and the ratio of these two values is used as a marker of inflammation.[13-16]

During inflammation, changes occur in the proportion of circulating leukocytes. The increase in neutrophils is accompanied by a finding of relative lymphopenia. Therefore, the neutrophil-lymphocyte ratio has been proposed as a simply calculable marker of inflammatory response. As stated in the study in the literature, neutrophil lymphocyte ratio was found to be compatible with prognosis when evaluated with sepsis scores such as APACHE 2 and SOFA. The neutrophil lymphocyte ratio is also called the neutrophil lymphocyte stress factor. There is an increasing number of studies showing that an increased neutrophil/lymphocyte ratio is associated with a poor prognosis in various diseases. For example, some studies have reported that the mortality rate in acute coronary syndrome is related to the neutrophil-lymphocyte ratio.[17-18]

The presence of T lymphocytes in a tumor is an indicator of the presence of an immune response against the mass. One study stated that a low lymphocyte count in colorectal tumors is a predictor of a poor prognosis. In studies by Blake-Mortimer et al.[20], the neutrophil-to-lymphocyte ratio was observed as a prognostic factor in colorectal and ovarian cancers.[19]

The peripheral blood neutrophil-to-lymphocyte ratio has been used as a parameter associated with physiologic stress and inflammation. Several studies have been used to evaluate its effect on mortality in oncologic errors. Öztürk et al.[21] reported a significant increase in the neutrophil-lymphocyte ratio in young patients with acute coronary syndrome. Studies by Kapçı et al.[22] and Kahramanca et al.[23] emphasized the importance of an increased neutrophil lymphocyte ratio in the diagnosis of acute appendicitis.

The prognostic importance of the neutrophil-lymphocyte ratio before treatment in various tumors has been investigated in many studies. The presence of systemic inflammatory reactions is used as a poor prognostic marker in various types of cancer.[24,25] In studies, the neutrophil-lymphocyte ratio was found to be high in patients with advanced ovarian cancer.[26-29] Furthermore, it is essential to develop novel methodologies and approaches, similar to those used in other medical conditions, to accurately identify cancer patients who are in a critical condition.[30]

CONCLUSION

In our study, high white blood cell count, high neutrophil count, decreased hemoglobin and hematocrit, and increased BUN and lactate levels seem to be predictors of mortality during emergency admissions in cancer patients.

ETHICAL DECLARATIONS

Ethics Committee Approval: This study is a specialty thesis in the field of emergency medicine. Before 2020, institutional approval was obtained, and ethics committee decisions were not taken for that period. All procedures performed in studies involving human participants were in accordance with the ethical standarts of the institutional and/or national research committee and with 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declared that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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